Supplemental Material

Widely Used Pesticides with Previously Unknown Endocrine Activity Revealed as *in vitro* Anti-androgens

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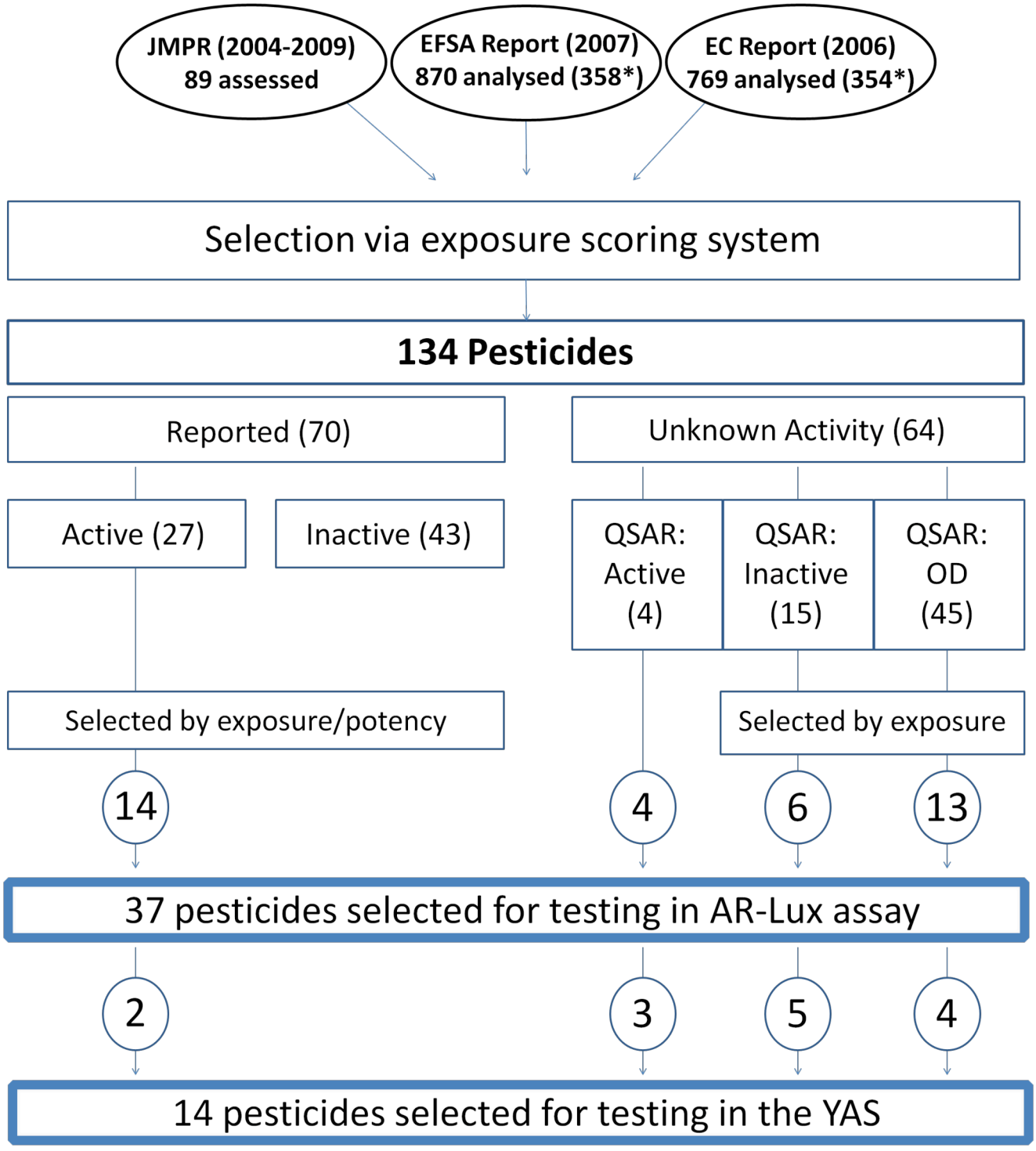
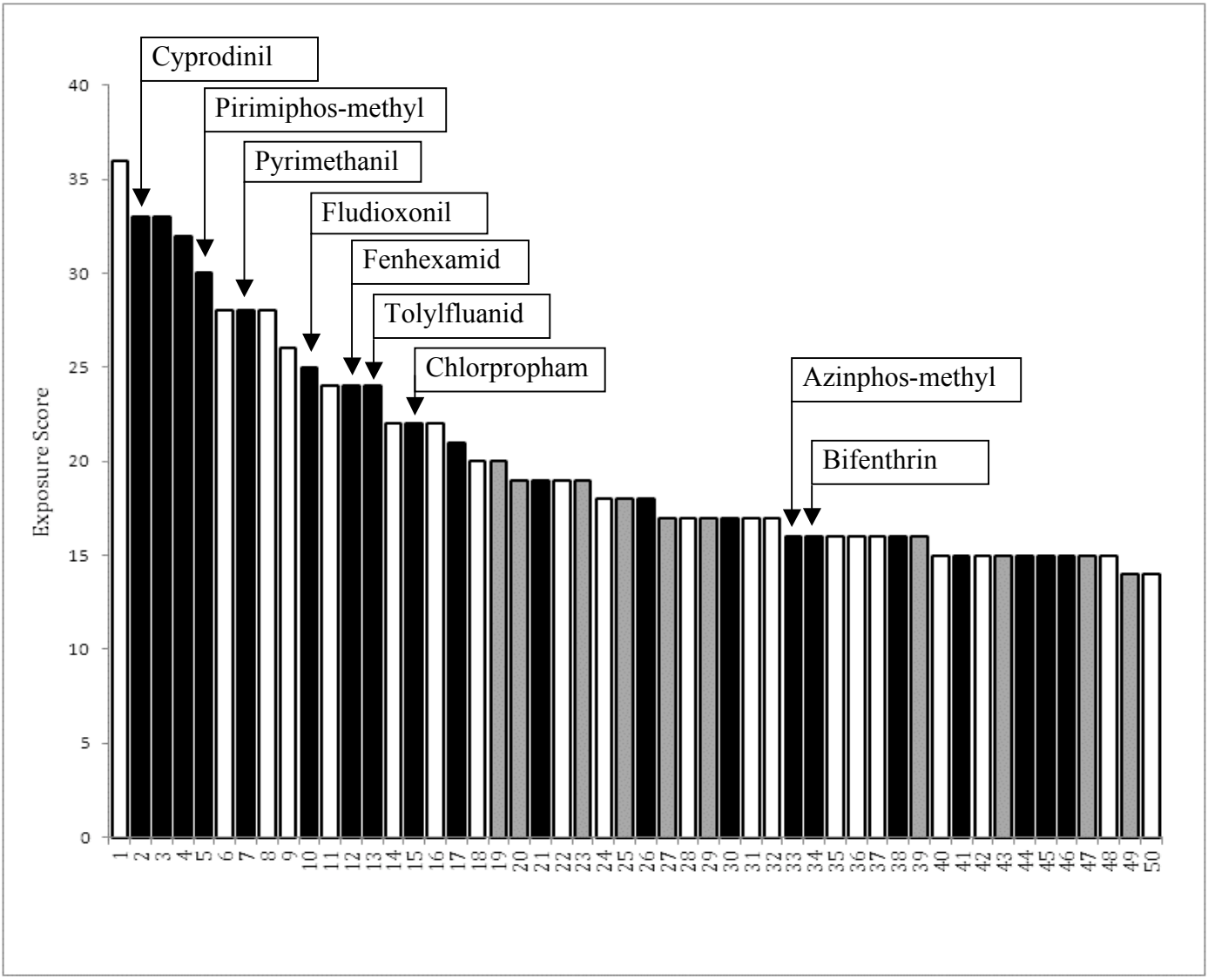


Supplemental material, Figure 1. Decision process used to select pesticides for testing receptor-mediated anti-androgenicity. * indicates the number of pesticides detected from the total number analysed for each data source, OD = Out of Domain.



Supplemental material, Figure 2. Pesticides ranked by total exposure score. Solid bars indicate anti-androgenic pesticides, clear bars indicate known inactive androgen receptor antagonists and grey bars indicate unknown activity on the androgen receptor. Indicated pesticides refer to newly described anti-androgenic activity (in at least one asssay). Numbers on *x* axis refer to individual pesticides and names of corresponding pesticides are as follows:

Number	Pesticide	Number	Pesticide	Number	Pesticide
1	maneb group	18	cypermethrin	35	indoxacarb
2	cyprodinil	19	methoprene	36	methomyl
3	procymidone	20	Boscalid	37	spinosad
4	imazalil	21	endosulfan	38	tebuconazole
5	pirimiphos-methyl	22	glyphosate	39	zolfo
6	malathion	23	maleic hydrazide	40	carbendazim
7	pyrimethanil	24	mandipropamid	41	dicofol
8	thiabendazole	25	phosphine	42	diquat
9	imidacloprid	26	prochloraz	43	dithianon
10	fludioxonil	27	diphenylamine	44	lambda-cyhalothrin
11	azoxystrobin	28	folpet	45	myclobutanil
12	fenhexamid	29	mepiquat	46	pp-DDE
13	tolylfluanid	30	methiocarb	47	pp-dichlorbenzophenone
14	bromide(methyl)	31	pyraclostrobin	48	triadimefon
15	chlorpropham	32	spirotetramat	49	formetanate
16	propamocarb	33	azinphos-methyl	50	phosmet
17	ortho-phenylphenol	34	bifenthrin		

Supplemental material, Table 1. Exposure scoring for pesticides.

Max residue EU (mg/kg)[a]		Top 10 fruit/cereal list (1 score per hit)[b]		JMPR estimated intake (µg/kg/day)[c]		EFSA report on commonly detected pesticides (%)[d]	
Value	Score	Value	Score	Value	Score	Value	Score
> 4	10	22+	10	> 0.01	10	> 5	10
3.5-3.9	9	19-21	9	0.007-0.0099	9	4-4.9	9
3-3.4	8	16-18	8	0.004-0.0069	8	3-3.9	8
2.5-2.9	7	13-15	7	0.001-0.0039	7	2-2.9	7
2-2.4	6	10-12	6	0.0007-0.00099	6	1-1.9	6
1.5-1.9	5	7-9	5	0.0004-0.00069	5	0.8-0.9	5
1-1.49	4	4-6	4	0.0001-0.00039	4	0.7-0.79	4
0.5-0.99	3	3	3	0.00007-0.000099	3	0.6-0.69	3
< 0.5	2	2	2	0.00004-0.000069	2	0.5-0.59	2
detected > 4	2	1	1	< 0.00004	1	0.4-0.49	1
detected 1-4	1	0	0			< 0.4	0
not listed	5	not listed	0	not listed	5	not listed	5

a. Refers to the maximum residue found in any food commodity in the European Union (European Comission 2009), b. Refers to the number of times a pesticide was listed in the top 10 most common pesticide from each country (European Comission 2009), c. Refers to the estimated daily intake from the Joint FAO/WHO meeting on pesticide residue reports (WHO 2009), d. Refers to the percentage of times each pesticide was detected during routine testing of fruits and vegetables in Europe (EFSA 2009).

Supplemental material, Table 2. Comparison between anti-androgenicity and exposure scores by Environmental Relevance Ratio (ERR).

	Anti-androg.[a]	**Exposure scoring[b]**					**ERR[c]**	
Pesticide	**IC20 (µM)**	**a**	**b**	**c**	**d**	**total**	**Total/IC20**	**ADI[d]/IC20**
Procymidone	*0.163*	*10*	*9*	*5**	*9*	*33*	*202.5*	*52.67*
Fenitrothion	*0.098*	*2*	*1*	*8*	*0*	*11*	*112.2*	*0.55*
Vinclozolin	*0.163*	*3*	*2*	*5**	*3*	*13*	*79.8*	*48.41*
Dimethomorph	0.263	2	0	4	6	12	45.6	6.22
Fludioxonil	0.801	4	5	7	9	25	31.2	36.26
Bromopropylate	*0.54*	*4*	*1*	*5**	*3*	*13*	*24.1*	*0.89*
Fenhexamid	2.02	7	5	4	8	24	11.9	5.48
Dicofol	*1.43*	*5*	*1*	*5**	*4*	*15*	*10.5*	*2.71*
Imazalil	3.23	8	9	5	10	32	9.9	2.92
Prochloraz	*2.39*	*2*	*3*	*7*	*6*	*18*	*7.5*	*4.30*
Linuron	1.74	2	0	5*	5	12	6.9	0.26
Ortho-phenylphenol	3.43	2	6	5*	8	21	6.1	2.52
Tebuconazole	2.89	2	2	5	7	16	5.5	0.27
Pirimiphos-methyl	5.49	10	9	7	4	30	5.5	0.86
Endosulfan	*6.05*	*5*	*4*	*4*	*6*	*19*	*3.1*	*0.21*
Azinphos-methyl	*5.38*	*2*	*3*	*5**	*6*	*16*	*2.9*	*0.51*
Chlorpropham	7.66	2	4	10	6	22	2.9	0.35
Quinoxyfen	4.79	2	0	7	3	12	2.5	0.27
Methiocarb	6.82	8	1	3	5	17	2.5	0.02
Cyprodinil	15.1	8	8	7	10	33	2.2	0.20
Pyrimethanil	27.2	10	4	7	7	28	1.0	0.11
Ethoxyquin	*10.7*	*2*	*2*	*4*	*0*	*8*	*0.75*	*0.09*
Lambda-cyhalothrin	23.1	2	0	7	6	15	0.65	0.06

a = Anti-androgenicity based on MDA-kb2 assays. [b]Exposure scoring is according to supplemental material, Table 1 (a = maximum EU residue; b = top 10 fruit/cereal list; c = JMPR estimated intake; d = fruit/vegetable EFSA report), with total equals the sum of all four scores. [d]ADI is the adjusted theoretical daily intake for French population (µg/kg b.w./day), derived from Menard et al. (2008). Pesticides are ordered by their environmental relevance ratio (ERR), i.e. ratio between IC20 for anti-androgenicity and sum of all exposure scores. Pesticides in italics are no longer registered for use in Europe. * = indicates a "not listed" score of 5 (see methods).